

Richard J. Hodes, MD  
Director, National Institute on Aging  
Building 31, Room 5C27  
31 Center Drive, MSC 2292  
Bethesda, MD 20892

Re: NOT-AG-18-034

December 21, 2018

Dear Dr. Hodes,

The Endocrine Society appreciates the opportunity to comment on the National Institute of Aging (NIA) Aging Well in the 21st Century: Strategic Directions for Research on Aging. Founded in 1916, the Endocrine Society is the world's oldest, largest, and most active organization devoted to research on hormones and the clinical practice of endocrinology. Our membership of over 18,000 includes clinical, translational, and basic scientists making discoveries to enhance our understanding the role of hormones in healthy aging, as well as how the aging process affects endocrine systems and influences endocrine-related diseases.

We are pleased that the Strategic Directions document supports additional research to understand changing hormone biology during aging and the development of interventions, including hormone-based therapies, to address hormonal changes and the effects of aging more generally. We are also encouraged that NIA proposes to investigate brain-body interactions and how endocrine systems interact with the brain throughout aging in normal and in pathological states e.g., Alzheimer's Disease. These research areas are critically important as we seek to improve health throughout the lifespan and we urge NIA to preserve these topics in the final Strategic Directions document.

The development of safe and effective interventions is of paramount importance to the biomedical research enterprise, as described in objective C-1. However, the Endocrine Society is concerned about the misuse of hormones to counter the effects of aging, for example inappropriate growth hormone use and compounded "bioidentical" hormones for e.g. menopause. In addition to research on hormone therapy and the use of compounds to produce beneficial effects, attention should be paid to adverse effects, especially for existing practices that fall outside of FDA's regulatory authority. **We encourage NIA to continue to support research on hormonal therapies for aging, with attention to both efficacy and adverse effects, to help combat harmful practices that may exist.**

Although the Strategic Directions document correctly emphasizes the importance of endocrinology in the context of intervention-driven goals (e.g., goals C, D, E, and F), we note that there is not a corresponding emphasis on fundamental mechanistic insights into hormone biology and aging in the section on "Understanding the Dynamics of the Aging Process". Endocrine researchers, including many funded by the NIA, are making important discoveries in areas with direct relevance to aging populations such as thyroid biology, bone and mineral metabolism, diabetes and metabolic disease, and the role of vitamin D



in aging-related processes. **We therefore recommend that goal A include an additional objective that details the need to better understand the influence of endocrine signaling and hormonal networks, including sexual dimorphism, on the aging process.** This objective could reference the importance of understanding homeostatic hormone systems in the context of healthy aging and how altered endocrine signaling contributes to diseases throughout the aging process.

Additionally, we are mindful of the fact that the single greatest risk factor for cancer is increasing age. In this context, the Strategic Directions document recognizes the need to develop interventions to address the risk of developing diseases such as cancer with increasing age, and that cancer susceptibility in older adults may include health disparities that must be addressed. These objectives would be further strengthened by a better understanding of the fundamental changes associated with aging that increase cancer susceptibility. **We recommend that the biology of aging and cancer be included as a component of objective A-3;** this could also be accomplished in cooperation with other NIH Institutes and Centers.

We recognize all of the objectives built into Goal B include important endocrine components. For example, understanding the relationship between mental health factors and cortisol during aging could be useful as NIA seeks to identify non-invasive/minimally invasive methods to measure biomarkers to monitor healthy aging as described in B-2. Many of the long-term health effects from environmental exposures described in B-3 include alterations in endocrine pathways due to endocrine-disrupting chemicals (EDCs). **As such, it will be important to capture information on hormonal status in research studies consistent with the objectives in Goal B, and, in particular, for longitudinal studies supported by NIA.**

The Endocrine Society welcomes the ambitious roadmap described in “Aging Well in the 21st Century: Strategic Directions for Research on Aging” and we look forward to contributing to the scientific goals described in the document. We believe that with an additional emphasis on fundamental research on hormone biology and endocrine signaling, the document will better guide researchers funded by NIA towards interventions that will improve public health for populations throughout the lifespan. Thank you for considering the Endocrine Society’s comments. If we can be of further assistance, please contact Joseph Laakso, Director of Science Policy at [jlaakso@endocrine.org](mailto:jlaakso@endocrine.org).

Sincerely

Susan Mandel, MD  
President, Endocrine Society